# Bilirubin metabolism and Jaundice-2

By

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**Lecturer of Medical Biochemistry**

# INTENDED LEARNING OBJECTIVES (ILOs)

**By the end of this lecture the student will be able to:**

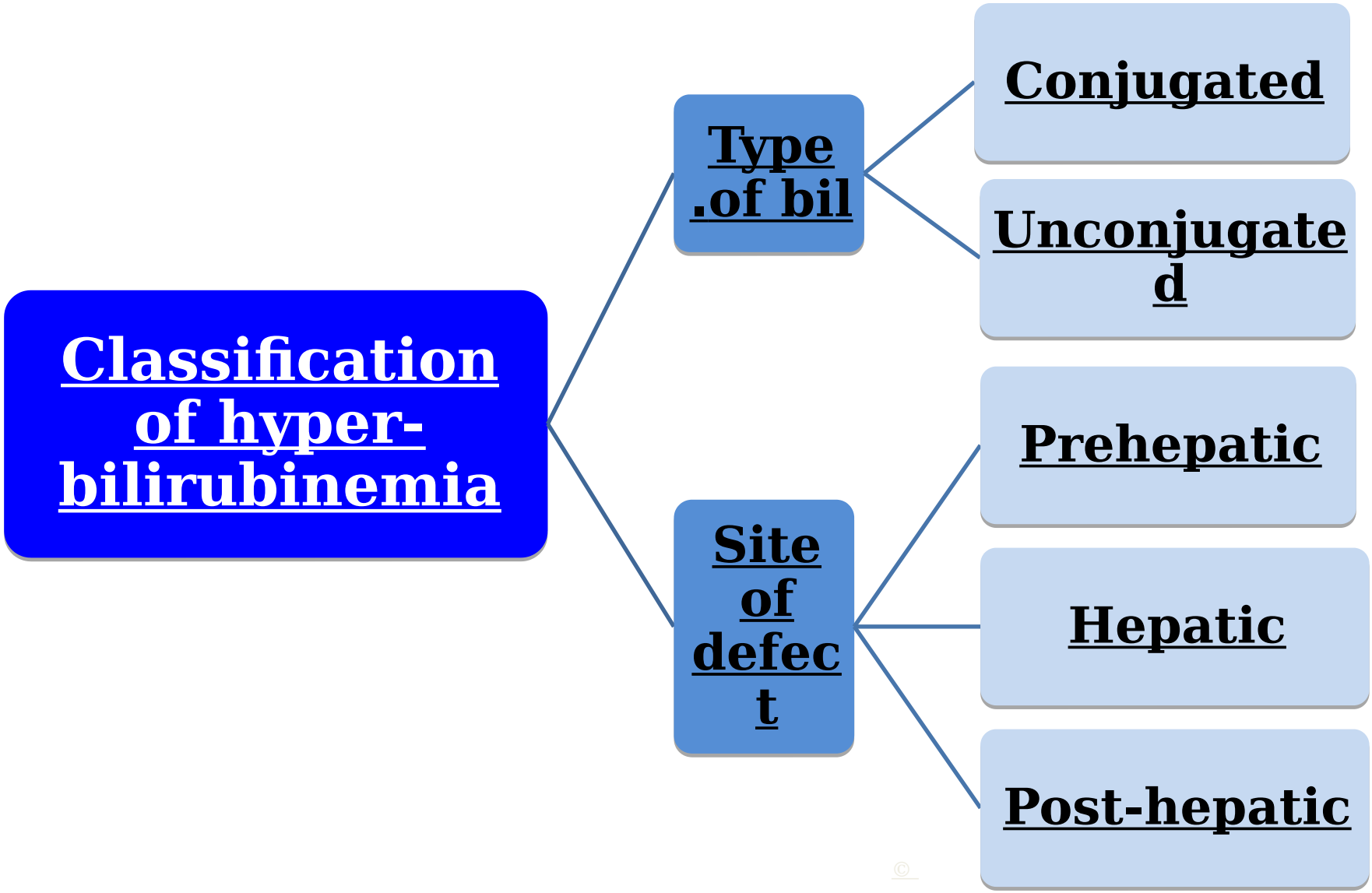
1. **Distinguish different types of jaundice**
2. **Interpret laboratory findings of different types of jaundice**

# Outlines

- What are  different types of  jaundice
- Prehepatic jaundice
- Hepatic jaundice
- Post-hepatic jaundice


JAUNDICE

# What are  different types of  jaundice


Classification of hyper-bilirubinemia
Type .of bil
Conjugated
Unconjugated
Site of defect
Prehepatic
Hepatic
Post-hepatic

# Classification of hyper-bilirubinemia according to site of defect

## A- Prehepatic

- Hemolytic
- Neonatal jaundice

## B- Hepatic

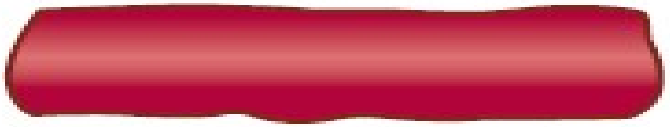
- Hepatocellular damage
- Crigler-Najjar syndromes I & II
- Gilbert syndrome
- Dubin–Johnson syndrome
- Rotor syndrome

## C- Post-hepatic

- Obstruction of the biliary tree

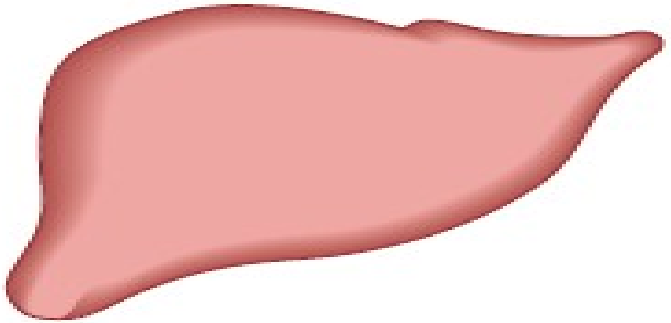
# Classification of hyper-bilirubinemia according to site of defect

PRE-HEPATIC
(Vascular)



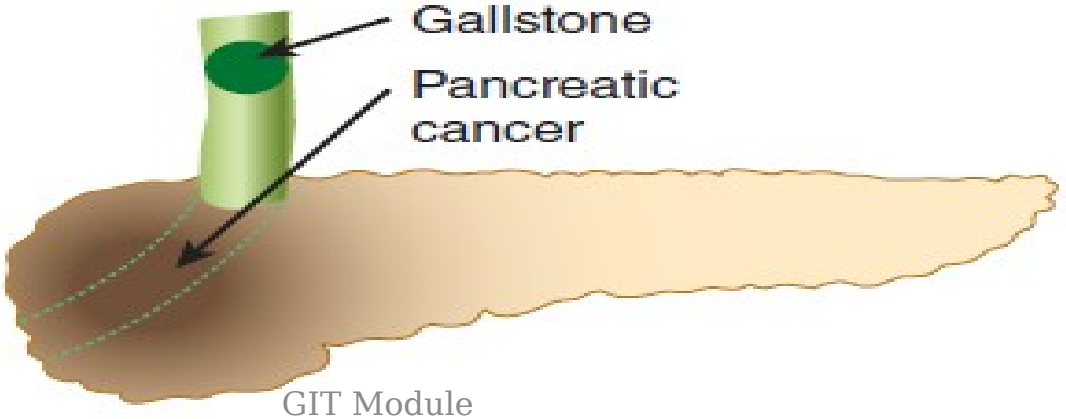
Hemolytic anemias

HEPATIC
(Liver)



Liver diseases
(eg, hepatitis, cancer)

POST-HEPATIC
(Biliary system & pancreas)

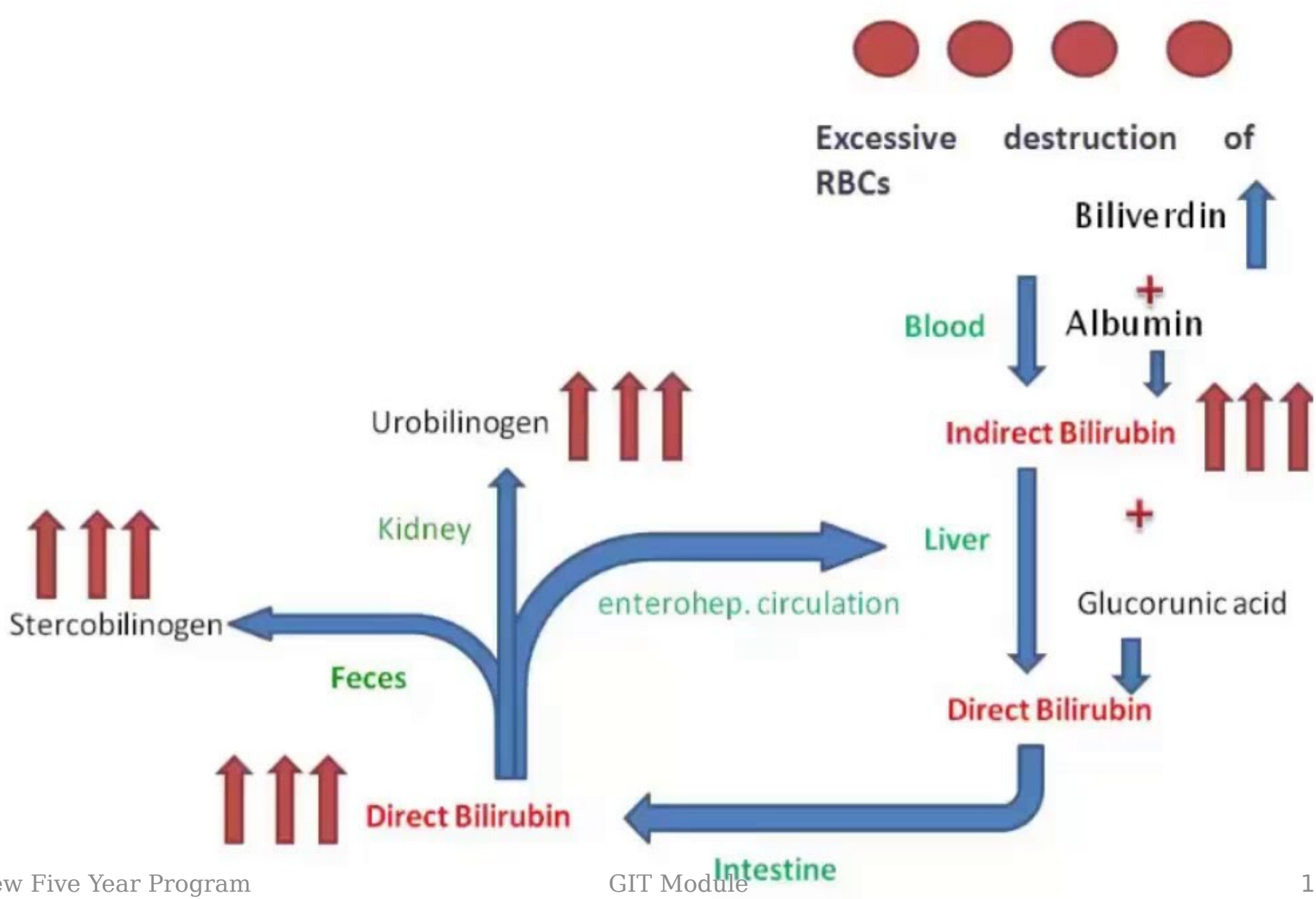


# A- Prehepatic Jaundice

**Hemolytic -1 jaundice**

**Neonatal jaundice -2**

# 1) Hemolytic Jaundice



# 1- Hemolytic Jaundice (Retention hyperbilirubinemia)

**Due to overproduction of bilirubin**

**Causes:**

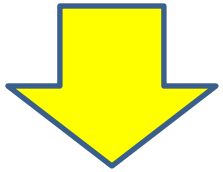
- **In neonates: Rh incompatibility between maternal and fetal blood.**

- **In children and adults: e.g G-6-PD deficiency, or pyruvate kinase defeciency or sickle cell anemia.**

# 1- Hemolytic Jaundice

**Extensive hemolysis produce bilirubin faster than it can be conjugated:**

- **UCB in the blood increases,**
- **More CB is made and excreted into the bile,**
- **The amount of urobilinogen entering the enterohepatic circulation is increases**
- **Urinary urobilin and stercobilin increases**



**Jaundice, normal color of urine and stool**

# 2- Neonatal “Physiological Jaundice”

**Transient**

**hyperbilirubinemia**

## Causes:

**Due to accelerated hemolysis and an immature hepatic system for the uptake, conjugation, and secretion of bilirubin**

# 2- Neonatal “Physiological Jaundice”

- **UCB in the blood increases more than the binding capacity of albumin (20–25 mg/dl) (acholuric jaundice)**
- **UCB cross the blood-brain barrier, cause toxic encephalopathy (kernicterus)**
- **If left untreated, may result in mental retardation**

# 2- Neonatal “Physiological Jaundice”

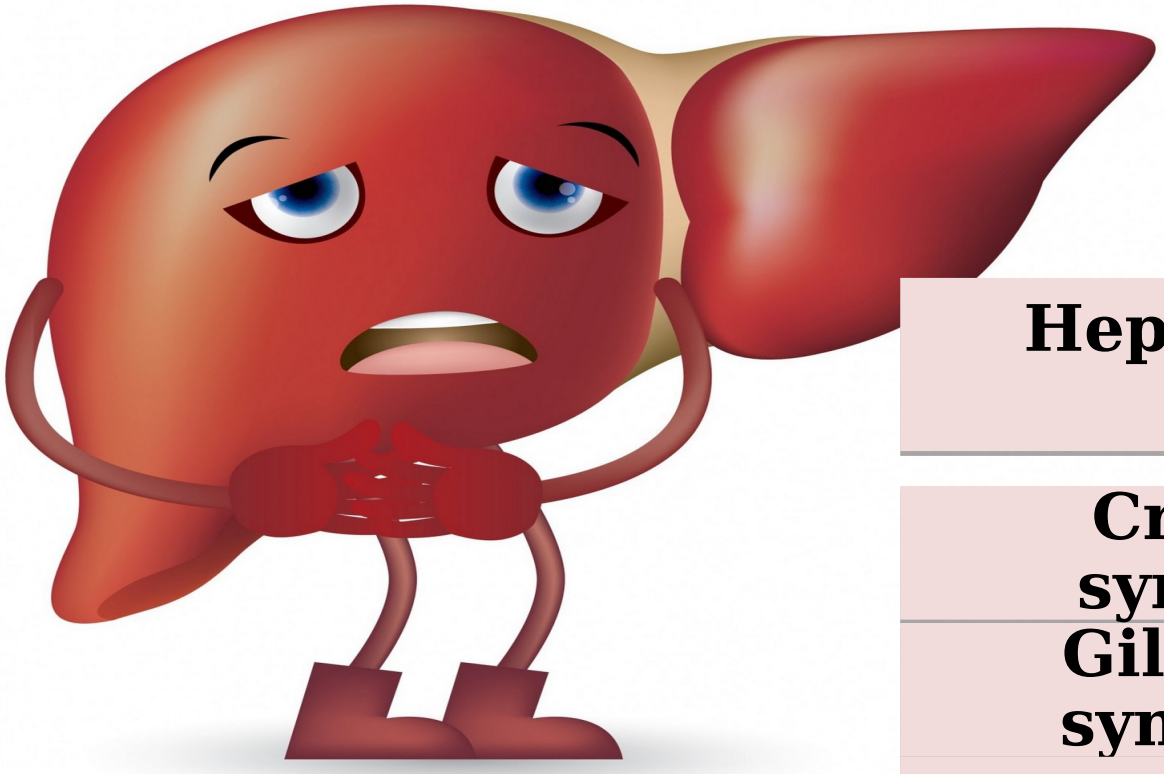
## Treatment:

**1- Phototherapy (blue light): converts bilirubin to more polar water-soluble isomers**

**2- Barbiturates: induction of bilirubin UDP-glucuronosyl transferase enzyme**

# Hepatic Jaundice

# B- Hepatic Jaundice



**Hepatocellular -1 damage**

**Crigler-Najjar -2 syndromes I & II**

**Gilbert -3 syndrome**

**Dubin–Johnson -4 syndrome**

**Rotor -5 syndrome**

# 1- Hepatocellular damage

**Causes:**

**Toxins, drugs, hepatitis viruses and cirrhosis**

**Damage to liver cells and decreased conjugation capacity**

**Increase of UCB levels the blood**

**Inflammatory oedema of hepatocytes with compression of the intracellular canaliculi "mild obstruction"**

**Increase of CB levels the blood**

# 2- Crigler-Najjar syndrome

- **It occurs due to mutation in the gene encoding UDP-glucuronyl-transferase enzyme**

**Type I Crigler-Najjar: syndrome:** **Complete absence of the enzyme activity**

**Type II Crigler-Najjar: syndrome:** **Partial absence of the enzyme activity (about 10% of the enzyme activity retained)**

# Type I Crigler-Najjar syndrome:

- **Autosomal recessive disorder due to mutation in the gene encoding UDP-glucuronyl-transferase enzyme**
- **Complete absence of the enzyme activity**
- **Serum UCB usually exceeds 20 mg/dl**
- **Severe congenital jaundice and brain damage**
- **The disease is often fatal within the first 15 months of life**

## Treatment:

- **Phototherapy reduces plasma bilirubin levels**

# Type II Crigler-Najjar syndrome:

- **Autosomal dominant disorder due to mutation in the gene encoding UDP-glucuronyl-transferase enzyme**
- **Partial absence of the enzyme activity (typically <10% of normal)**
- **Serum UCB doesn't exceed 20 mg/dl**
- **Usually survives up to adulthood**

## Treatment:

- **phenobarbital treatment is effective, generally with a decrease of at least 25% in serum bilirubin**

# 3- Gilbert's syndrome

- **Autosomal dominant or recessive disorder due to mutation in the gene encoding UDP-glucuronyl-transferase enzyme**
- **Reduced activity of the enzyme (30% of normal activity is retained)**
- **Serum UCB doesn't exceed 5 mg/dl**
- **Episodes of jaundice may be triggered by stress**

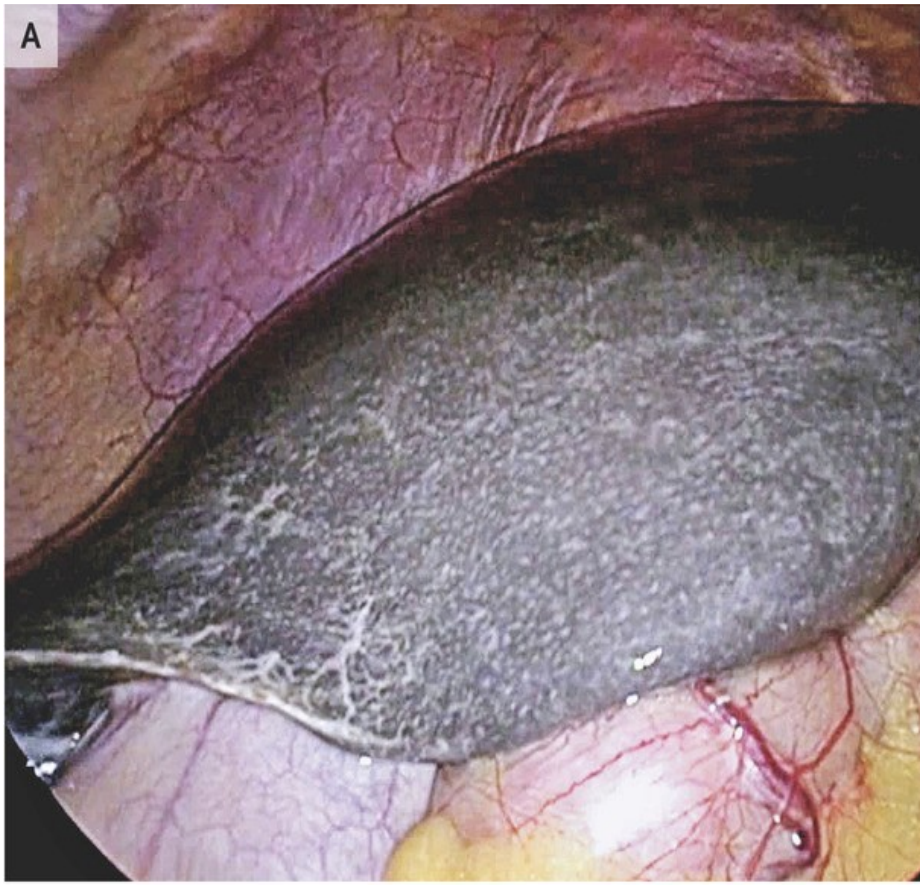
**Treatment:**

- **Very benign condition, NO treatment is needed**

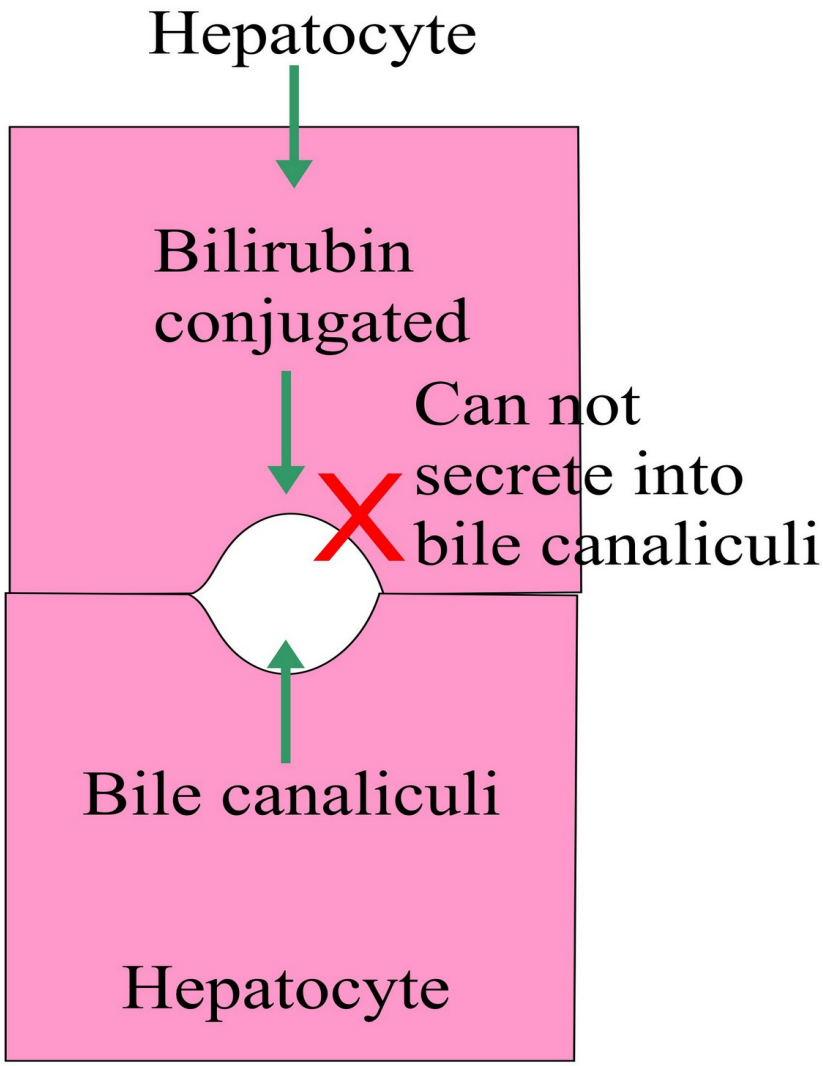
# 4- Dubin Johnson syndrome

- **Autosomal recessive disorder caused by mutations in the gene encoding the protein involved in the secretion of conjugated bilirubin into bile**
- **It causes a black liver due to the deposition of a dark pigment but not bilirubin**
- **Elevation of conjugated bilirubin**
- **A benign condition**

# 4- Dubin Johnson syndrome




**Liver with black pigmentation**



# 5- Rotor syndrome

- **Autosomal recessive disorder, but its cause has not been identified**
- **Similar to Dubin–Johnson syndrome, but the liver cells are not pigmented**
- **Elevation of conjugated bilirubin**
- **A benign condition**

**Impaired glucuronyl transferase activity is observed in all of the following except:**

**A.Gilbert syndrome**

**B.Crigler Najjar syndrome**

**C.Physiological jaundice**

**D.Dubin Johnson syndrome**

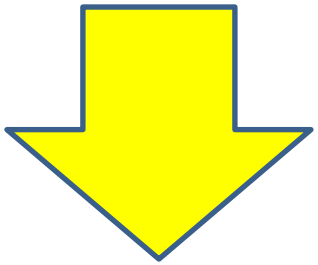
**E.Hepatocellular jaundice**

# Post-Hepatic (obstructive) Jaundice

# Obstructive Jaundice Regurgitation) (hyperbilirubinemia

**Due to obstruction of the hepatic or common bile ducts as in case of:**

- **Gall stones,**
- **Cancer head of pancreas**
- **Biliary cirrhosis,**
- **Hepatoma**



**Preventing passage of CB into the intestine**

# Obstructive Jaundice

**The liver "regurgitates" conjugated bilirubin into the blood**

**The conjugated bilirubin is excreted in the urine (choluric jaundice)**

**Urinary urobilinogen is absent**

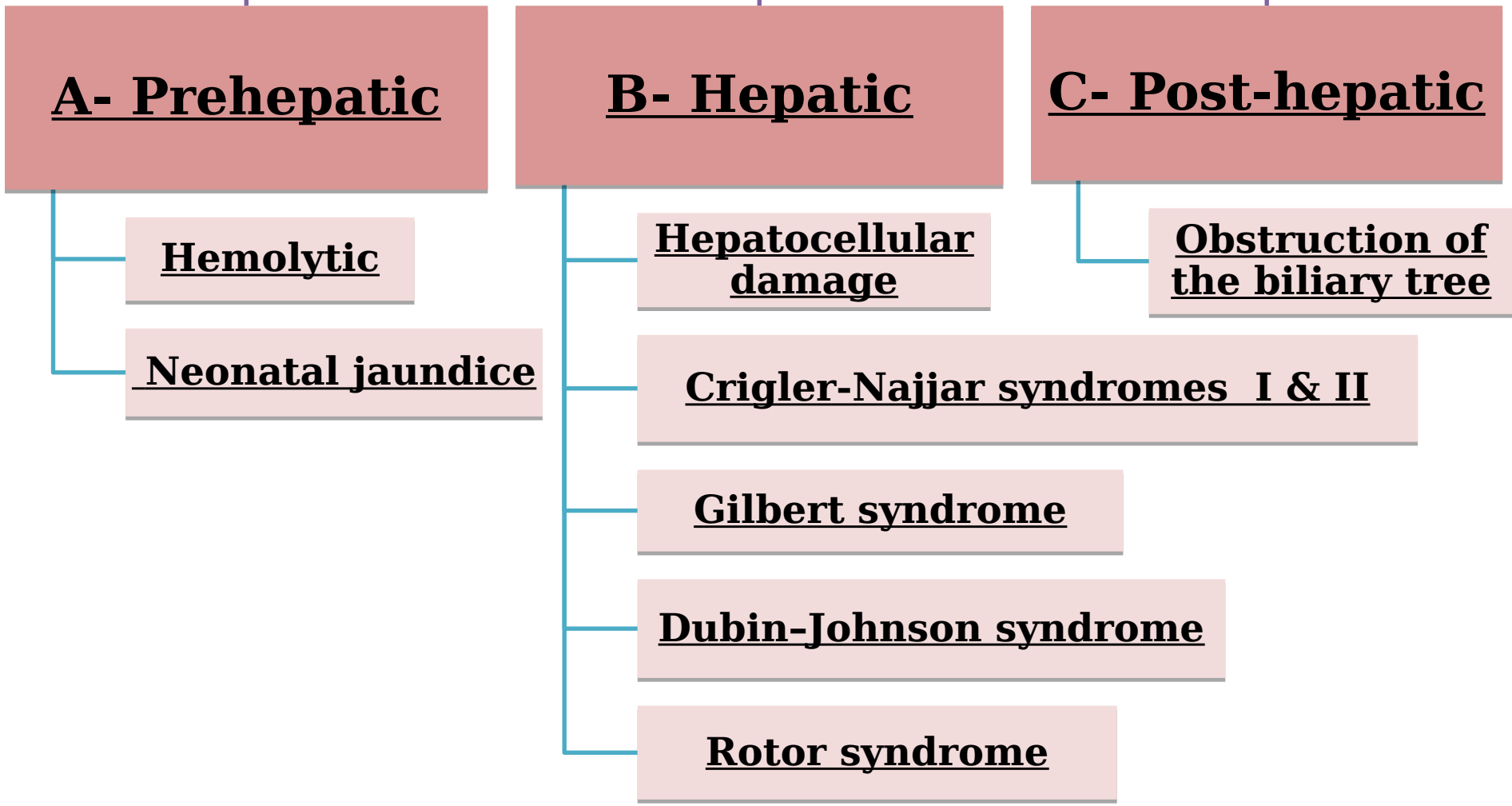
**Stool stercobilinogin is absent, giving a pale, clay colored stool**

# MCQ

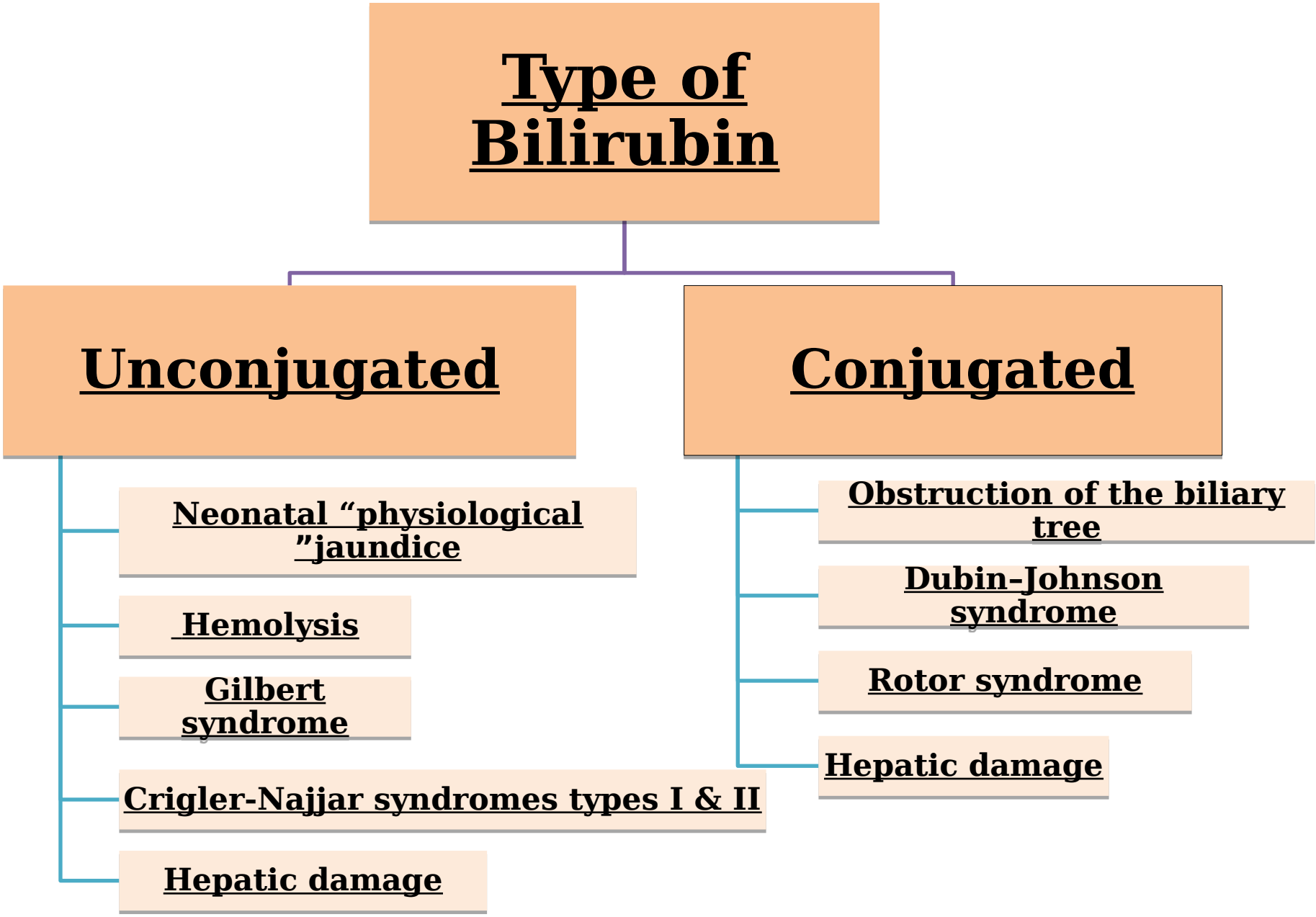
- **A rise in serum "direct" bilirubin would be expected in all of the following except:**

**1. hemolytic jaundice.**
**2. absence of glucuronyl transferase as in the newborn.**
**3. Gilbert's syndrome.**
**4. Type 1 Crigler-Najjar syndrome**
**5. biliary obstruction.**

# Classification of hyper-bilirubinemia according to site of defect



| jaundice Obstruction of bile duct | Defect in conjugation and/or excretion of bilirubin in bile | | | Increase bilirubin production | |
|---|---|---|---|---|---|
| Biliary stones Cancer head of pancreas | 1.Gilbert syndrome 2.Crigler-najjar syndrome | Dubin-johnson syndrome Rotor syndrome | Hepatic damage e.g; Hepatitis | 1.Hemolysis of RBCS as in sickle cell anemia, G6PD deficiency and RH incompatibility 2.Neonatal jaundice | Causes: |
| Direct (conjugated) | Indirect | Direct | Indirect + direct | Indirect (unconjugated) | Type of elevated bilirubin |
| Present (Choluric)<br><br>Absent | | | Present (Choluric)<br><br>Decrease | Absent (Acholuric) Normal color<br><br>Increase | <u>Urine</u><br>1.Presence of conjugated bilirubin (dark colored urine)<br>2.Urobilinogen |
| Pale clay colored and bulky(steatorrhea)<br><br>Absent | | | Pale clay colored<br><br>Decrease | Normal<br><br>Increase | <u>Stool</u><br>1.Color and consistency<br><br>2.Stercobilin |
| Normal<br>Increased<br>Present (itching) | | | Increased<br>.....<br>..... | Normal<br>.....<br>..... | <u>Blood test:</u><br>S. ALT and AST<br>Serum ALP<br>Serum bile salts |


Type of Bilirubin
Unconjugated
Neonatal “physiological ”jaundice
Hemolysis
Gilbert syndrome
Crigler-Najjar syndromes types I & II
Hepatic damage
Conjugated
Obstruction of the biliary tree
Dubin–Johnson syndrome
Rotor syndrome
Hepatic damage

# Summary

- **Hemolytic Jaundice (Retention hyperbilirubinemia) is due to overproduction of bilirubin**

- **Impaired glucuronyl transferase activity occurs in**

**Gilbert syndrome**
**Crigler Najjar syndrome**
**Physiological jaundice**
**Hepatocellular jaundice**

# Thank you

**Marwa Al**